Amendments to the Specification:

Please replace the paragraph beginning at page 8, line 32 and ending at page 9, line 3 with the following amended paragraph:

Figure 2 diagrams the construction of the antibody fusion constructs. The extracellular domain of RANTES or B7.1 obtained by polymerase chain reaction and the heavy chain variable region of the anti-tumor Ig are cloned on opposite ends of a flexible ~~region~~ linker (nucleotides 7 to 54 of SEQ ID NO: 11). (SEQ ID NO: 12 shows the amino acid sequence corresponding to SEQ ID NO: 11.) The resulting clone is cloned into a human IgG3 expression construct. The heavy chain IgG3 construct and a kappa light chain construct are transfected into Sp2/o Myeloma cells. The fusion protein is then secreted from the cells.

Please replace the paragraph beginning at page 9, line 4 and ending at page 9, line 10 with the following amended paragraph:

Figure 3 depicts the vector construction for the expression of RANTES.Her2.IgG3. RANTES was cloned at the 5' terminus of human IgG3 heavy chain through a flexible linker (nucleotides 13 to 60 of SEQ ID NO: 13) maintaining the open reading frame of the fusion protein. (SEQ ID NO: 14 shows the amino acid sequence corresponding to SEQ ID NO: 13.) After transfection of both anti-HER2/neu light chain and RANTES heavy chain fusion genes into myeloma cells, an H_2L_2 form of the antibody is assembled and secreted.

Please replace the paragraph beginning at page 11, line 6 and ending at page 11, line 20 with the following amended paragraph:

Figure 10 provides the structure of her2.IgG3 and B7.her2.IgG3 molecules. The heavy and light chain variable regions of humanized humAb4D5 anti-HER2/neu were cloned between the EcoRV sites and NheI sites of the mammalian expression vector for human IgG3 previously described (Coloma, M. et al., "Novel Vectors for the Expression of Antibody Molecules Using Variable Regions Generated by Polymerase Chain Reaction," *J*

Immunol Methods 152:89-104 (1992), which is hereby incorporated by reference). For the construction of B7.her2.IgG3, the B7.1 leader and extracellular domain were joined to the $(Ser\text{-}Gly_4)_3$ linker sequences (nucleotides 7 to 54 of SEQ ID NO: 11) which had been fused to the amino terminus heavy chain variable sequences of the her2.IgG3 antibody. A schematic diagram of the secreted H_2L_2 forms of control her2.IgG3 and B7.her2.IgG3 are also shown.

Please replace the paragraph beginning at page 40, line 24 and ending at page 41, line 20 with the following amended paragraph:

Antibody Expression vectors: For the construction of a humanized Her2.IgG3 antibody, the variable light and heavy chain sequences were obtained from the humanized humAb4D5-8 antibody (kindly provided by Dr. P. Carter, Genentech Inc., San Francisco, CA) (Carter, P., et al., "Humanization of an Anti-p185HER2 Antibody for Human Cancer Therapy", *Proc Natl Acad Sci USA*, 89:4285-9 (1992); Rodrigues, M.L., et al., "Engineering a Humanized Bispecific F(ab')2 Fragment for Improved Binding to T Cells," *Int J Cancer Suppl*, 7:45-50 (1992), which are hereby incorporated by reference) and cloned into previously described mammalian expression vectors for human kappa light chain and IgG3 heavy chains, respectively (Shin, S.U., et al., "Expression and Characterization of an antibody binding specificity Joined to Insulin-like Growth Factor-1: Potential Applications for Cellular Targeting", *Proc Natl Acad Sci USA*, 87:5322-6 (1990), which is hereby incorporated by reference). To construct RANTES.Her2.IgG3, human RANTES sequences were amplified from the plasmid pBS-RANTES (a generous gift from T. Schall ChemoCentryx, Mountain View, CA) using the sense primer 5'- GGCATAAGCTTGATATCTGAAGCCATGGGC-3' (SEQ ID No. 1) and antisense primer 5'- GCGCGGTTAACCGTTATCAGGAAAATGC-3' (SEQ ID No. 2), and the PCR product was subcloned as a HindIII/HpaI fragment at the 5' end of a cassette encoding the $(Ser\text{-}Gly_4)_3$ linker sequences (nucleotides 13 to 60 of SEQ ID NO: 13) fused to the anti-HER2/neu V_H sequences. The resulting RANTES-linker-V_H coding sequences were isolated as an EcoRV/NheI fragment and cloned into an expression vector for human IgG3 heavy chain (Coloma, M.J., et al., "Novel vectors for the Expression of Antibody Molecules Using Variable Regions Generated by Polymerase Chain Reaction," *J Immunol Methods*, 152:89-104 (1992), which is hereby incorporated by reference).

Please replace the paragraph beginning at page 45, line 3 and ending at page 45, line 24 with the following amended paragraph:

The antibody fusion protein RANTES.Her2.IgG3 was designed and constructed so that the chemokine RANTES was linked to the amino terminus of the heavy chain of the humanized anti-HER2/neu heavy chain antibody via a $(Ser\text{-}Gly_4)_3$ flexible linker (nucleotides 13 to 60 of SEQ ID NO: 13) (See Figure 3). Expression vectors encoding the anti-HER2/neu light chain and the RANTES.Her2.IgG3 heavy chain were transfected into Sp2/0 myeloma cells, and stable transfectants identified and expanded. Recombinant protein was purified using a protein G affinity column. Assembly and secretion of the H_2L_2 form of the recombinant fusion protein was verified by SDS-polyacrylamide gel electrophoresis. A complete H_2L_2form (~185 kDa) of the RANTES.Her2.IgG3 fusion protein is secreted by the myeloma cells (Figure 4A, lane 2). Following reduction of 2-mercaptoethanol, both RANTES.IgG# heavy chain (Figure 4A, lane 4), which has higher apparent MW than the IgG3 heavy chain (Figure 4A, lane 3) and intact anti-HER2/neu light chain (~25 kDa) were detected. Both Her2.IgG3 and RANTES.Her2.IgG3 recombinant antibodies were detected with an anti-human IgG antibody (Figure 4B), whereas only RANTES.Her2.IgG3 was specifically detected with an anti-RANTES antibody (Figure 4C).

Please replace the paragraph beginning at page 52, line 28 and ending at page 53, line 12 with the following amended paragraph:

Anti-HER2/neu B7.her2.IgG3 fusion heavy chain expression vector: The extracellular domain of the human B7.1 including the leader sequences were amplified using the primers 5'-GGCATAAGCTTGATATCTGAAGCCATGGGC-3' (SEQ ID No. 1) and 5'-GCGCGGTTAACCGTTATCAGGAAAATGC-3' (SEQ ID No. 2), and cloned as a HindIII/HpaI fragment at the 5' end of the $(Ser\text{-}Gly_4)_3$ linker sequences (nucleotides 7 to 54 of SEQ ID NO: 11) into a pUC19-flex plasmid. The V_H domain of the humanized humAb4D5-8 antibody was amplified by polymerase chain reaction from the plasmid pAK19 using primers 5'-GGCGGCGGATCCGAGGTTCAGCTGGTG-3' (SEQ ID No. 10) and 5'-TTGGTGCTAGCCGAGGAGACGGTGACCAG-3' (SEQ ID No. 9), digested with BamHI and HpaI and cloned at the 3' end of the B7.1 and flexible linker sequences. The resulting

insert encoding the B7.1-linker-V_H sequences was isolated as an EcoRV/NheI fragment and cloned into the expression vector for the IgG3 heavy chain (Coloma, M. et al., "Novel Vectors for the Expression of Antibody Molecules Using Variable Regions Generated by Polymerase Chain Reaction," *J Immunol Methods* 152:89-104 (1992), which is hereby incorporated by reference).

Please replace the paragraph beginning at page 55, line 21 and ending at page 56, line 17 with the following amended paragraph:

The expression vectors for the human IgG3 heavy and kappa light chains were previously described (Coloma, M. et al., "Novel Vectors for the Expression of Antibody Molecules Using Variable Regions Generated by Polymerase Chain Reaction," *J Immunol Methods* 152:89-104 (1992), which is hereby incorporated by reference). The variable domains of the anti-HER2/*neu* antibody were amplified by PCR from the plasmid pAK19 (kindly provided by P. Carter, Genentech Inc.) (Carter, P. et al., "High Level Escherichia Coli Expression and Production of a Bivalent Humanized Antibody Fragment," *Biotechnology (10)* 10:163-7 (1992), which is hereby incorporated by reference), and cloned into the corresponding heavy or light chain expression vectors to derive her2.IgG3. To construct a fusion antibody between her2.IgG3 and B7.1 (referred to as B7.her2.IgG3), the extracellular domain of human B7.1 was cloned at the 5'-end of the heavy chain variable region of her2.IgG3 (Figure 10). A flexible $(Ser\text{-}Gly_4)_3$ linker (nucleotides 7 to 54 of SEQ ID NO: 11) was provided at the fusion site of the recombinant fusion protein to facilitate correct folding of both antibody and B7.1 domains. B7.1 was expressed at the amino terminus of the heavy chain because B7.1 fused to the carboxyl terminus of the C_H3 domain showed decreased affinity for CD28. These results are consistent with a critical role of the amino terminus of B7.1 in mediating its biological activity (Guo, Y. et al., "Mutational Analysis and an Alternatively Spliced Product of B7 Defines its CD28/CTLA4-Binding Site on Immunoglobulin C-Like Domain," *J Exp Med* 181:1345-1355 (1995), which is hereby incorporated by reference). The light chain and either the her2.IgG3 or B7.her2.IgG3 heavy chain expression vectors were contransfected into Sp2/0 myeloma cells and stable transfectants secreting soluble proteins identified by ELISA.

Amendments to the Drawings

The attached sheet of drawings includes changes to FIG. 2. This sheet replaces the original sheet including FIG. 2. In FIG. 2, the nucleotide sequence "ACC", which was incorrectly identified as encoding the amino acid asparagine (Asn), has been amended to "AAC" which is the correct codon for Asn.